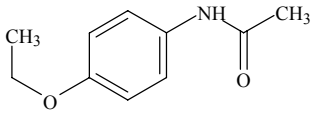
ANALGESIC MIXTURES CONTAINING PHENACETIN*

First Listed in the *Fourth Annual Report on Carcinogens*



CARCINOGENICITY

Analgesic mixtures containing phenacetin are *known to be human carcinogens* based on sufficient evidence of carcinogenicity in humans (IARC V.13, 1977; IARC V.24, 1980; IARC S.4, 1982; IARC S.7, 1987). Many case reports have indicated that abuse of analgesic mixtures containing phenacetin induces increased incidences of papillary necrosis, adenocarcinomas of the renal parenchyma, transitional cell carcinomas or papillomas of the renal pelvis, and urinary bladder carcinomas.

An IARC Working Group reported that there is limited evidence of carcinogenicity of analgesic mixtures containing phenacetin in experimental animals (NCI 67, 1978; IARC S.4, 1982; IARC S.7, 1987). When administered orally, a mixture of aspirin, phenacetin, and caffeine induced increased incidences of benign and malignant carcinomas of the urinary tract in mice and rats (IARC, S.7, 1987). A mixture of phenacetin and caffeine or phenacetin alone induced renal pelvic tumors and urinary bladder tumors in male rats. Half of the rats treated with phenacetin, phenazone, and caffeine in combination developed hepatomas (IARC S.4, 1982; IARC S.7, 1987).

PROPERTIES

The variety of substances and mixtures precludes a concise description of properties. Various pharmacopoeias give specifications for analgesic mixtures containing phenacetin. Grades available before 1983 contained 98%-101%, or 94%-106% phenacetin on a dried basis with 0.03% maximum *p*-chloroacetanilide. Also available was a tablet containing 150 mg phenacetin, 230 mg aspirin, and 15 or 30 mg caffeine or 230 mg aspirin, 30 mg caffeine, and 8, 15, 30, or 60 mg codeine phosphate.

USE

Analgesic mixtures containing phenacetin were previously used as prescription and over-the-counter drugs for mild-to-moderate pain associated with the musculoskeletal system. Such mixtures have been used for more than 80 years (IARC V.13, 1977).

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* There is no separate CAS registry number assigned to these mixtures. Phenacetin is included separately in this Report in Section III.B.

PRODUCTION

FDA reported that analgesic mixtures containing phenacetin are not currently manufactured in or imported into the United States. No data on historical production, imports,or exports were available.

EXPOSURE

The primary routes of potential human exposure to analgesic mixtures containing phenacetin are ingestion, inhalation, and dermal contact. Potential consumer exposure could have occurred through ingestion of analgesic mixtures containing phenacetin as pharmaceuticals. Mixtures with phenacetin usually contained 150 to 200 mg phenacetin (IARC V.13, 1977). Potential occupational exposure could have occurred through inhalation and dermal contact for workers involved in manufacturing, formulating, packaging, or administering the pharmaceuticals.

REGULATIONS

Analgesic mixtures containing phenacetin are not regulated by EPA because they are used as pharmaceuticals and in low quantities relative to other chemicals. However, there may be a small pollution problem relative to hospital wastes. FDA regulates these mixtures under the Food, Drug, and Cosmetic Act (FD&CA) and the Public Health Service Act as over-the-counter (OTC) drugs. FDA also regulates the labeling of all drugs containing phenacetin under FD&CA. OSHA regulates analgesic mixtures containing phenacetin under the Hazard Communication Standard and as chemical hazards in laboratories. It is listed as a medication that a physician and employer may wish to review. Regulations are summarized in Volume II, Table A-4.